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REMARKS

Status of the Application:

Claims 1-18 are pending in the application. Claims 12-14 are withdrawn subject to a restriction requirement. Claims 2, 4, 16, and 17 have been cancelled. Claims 1, 5, 6, 8, 9, 15, and 18 have been amended and no claims have been added. Accordingly, upon entry of the instant amendment, claims 1, 3, 5-11, 15, and 18 will be pending.

Rejections Under 35 USC §102:

Claims 1-3, 15, 17, and 18 were rejected under 35 USC § 102(b) as being anticipated by US Patent No. 6,150,345 ("345 patent"). Claims 2, 4, 16 and 17 having been cancelled by this amendment, the rejections are moot with respect to these claims.

According to the Office Action, the '345 patent teaches a tissue culture system comprising at least one isolated neural cell expressing at least one LPA receptor, a LPA, and a basal medium, as in claim 1. As noted by the Examiner (Office Action, page 6), '345 teaches sciatic nerve isolated from rat pups.

Claim 1 has been amended herein to recite *inter alia* the limitation of cancelled claim 4, as shown:

A tissue culture system comprising:

(a) at least one neural stem/progenitor cell isolated from subependymal zone or hippocampus, expressing at least one LPA receptor;

(b) a lysophosphatidic acid (LPA) compound selected from the group consisting of LPA 20:6, 18:1 (oleoyl), 16:0 (palmitoyl), and 14:0 (myristoyl) at a concentration range from 1 µM to 50 µM; and

(c) a basal culture medium comprising insulin and methyl cellulose, but free of EGF or FGF2.

(Emphasis added.)

Similarly, claim 15 has been amended to recite the "stem/progenitor cell" limitation of cancelled claim 16.

Applicants submit that the '345 patent describes tissue culture systems suitable for use with myelin producing cells, and that '345 neither teaches, suggests, nor even mentions a tissue culture system comprising a neural stem/progenitor cell, as instantly claimed in claims 1 and 15, and claims dependent thereon. In view of these amendments, reconsideration and withdrawal of the rejection of claims 1, 3, 15, 17, and 18 is respectfully requested.

Claims 1-11, and 15-18 were rejected under 35 USC § 102(e)(1) as being anticipated by US Patent Application Publication US2004/0014662 ("662 publication"). Claims 2, 4, 16 and 17 having been cancelled by this amendment, the rejections are moot with respect to these claims.

According to the Office Action (page 7), '662 teaches culturing neural stem cells in a neurosphere culture medium, which contains DMEM/F12, B27 supplement, HEPES and 20 ng/ml EGF.

As amended herein, claims 1 and 15 recite a basal culture medium that is "free of EGF or FGF2." By contrast, the '662 application teaches using "Neurosphere medium" containing either EGF, or both EGF and bFGF (FGF2), as described, e.g., on page 22, Example 3, paragraphs [0218, 0219].

The '662 publication does not teach or suggest a tissue culture system suitable for supporting neural stem/progenitor cells, in which the system is free of the growth factors EGF or FGF2, as claimed. As fully described in the specification, Applicants have developed a serum-free basal culture medium containing LPA that effectively supports growth of stem/progenitor cells and differentiation of neurospheres *in vitro* in the absence of growth factors such as EGF and FGF2. Such growth factors have been employed in prior art media formulations (see, e.g., specification page 5, lines 8-20; Example 6 on page 14; and Table 1, page 15).

Among the various unexpected advantages of the tissue culture system as claimed is the prolonged ability to maintain neurospheres in culture. For example, neurospheres can be cultured up to 3 months, as compared to 4-5 weeks in media supplemented with EGF + FGF2 (see, e.g., specification page 15, last paragraph

bridging page 16, line 2).

Thus, it is submitted that the instant claims are neither anticipated nor rendered obvious by the teachings of the '662 publication. Accordingly, reconsideration and withdrawal of the rejections of pending claims 1, 3, 5-11, 15, and 18 based on the '662 publication is respectfully requested.

Rejections Under 35 USC §112:

Claims 1-11 and 15-18 were rejected under 35 U.S.C. §112, first paragraph for alleged lack of enablement. Claims 2, 4, 16 and 17 having been cancelled by this amendment, the rejections are moot with respect to these claims.

The Office Action, at page 3, last paragraph, states that Applicant describes isolating "neurons" from subependymal zone and hippocampus, which can subsequently form neurospheres in the claimed culture conditions. In support of an alleged unpredictable effect of LPA on neurons, the Office Action (page 4) recites several examples in the art of LPA effects on several types of neurons including oligodendrocytes, Schwann cells and astrocytes.

As amended herein, independent claims 1 and 15 recite a "stem/progenitor cell isolated from the subependymal zone or hippocampus." Support for this limitation may be found, for example, in original claims 4 and 16, now cancelled. It is respectfully submitted that the teachings of the references cited by the Examiner, describing effects of LPA on various classes of neurons, do not provide support for unpredictability of LPA with respect to its effect on neural stem/progenitor cells, as claimed. Additionally, the claims as amended now recite a finite selection of LPA compounds, as fully described in the specification (see, e.g., page 7, line 21 through page 8, line 9), at a defined concentration range (as described on page 8, lines 28-29).

It is respectfully submitted that in view of the extensive teachings in the specification and the high level of skill in the art, one of ordinary skill would be required to exercise no more than routine experimentation in order to practice the invention over the full scope of the claims as amended.

The Office Action further states that Applicant is enabled to isolate neural stem/progenitor cells from a cadaver but fails to provide sufficient guidance as to how to obtain live neural tissue from a live embryonic tissue or a live postnatal tissue from a human without damaging the adult brain tissue or embryos.

Applicants respectfully disagree in part with the rejection, and submit that methods of obtaining brain samples from postnatal humans (children and adults), e.g., from specimens taken during brain surgery for various disorders, were well known in the art at the time of filing of the application. Accordingly, claim 8 has been amended to recite "postnatal or postmortem" human.

**CONCLUSION**

In view of the amendments and arguments presented herein, Applicants respectfully submit that pending claims 1, 3, 5-11, 15, and 18 are enabled, and accordingly respectfully request reconsideration, and withdrawal of the rejection.

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Respectfully submitted,

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